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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,730	01/02/2002	Robert M. Abrams	99-0137 (US02)	3733

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,730	ABRAMS ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-41,43,44,46,53-57 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-41, 43, 44, 46, 53-57, and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/4/06 has been entered.

Claims 32-41, 43, 44, 46, 53-57, and 59 remain pending and are under consideration in this Office Action.

Drawings

No drawings were filed with the application.

Claim Objections

Claim 41 is objected to because RGD is misspelled as "ROD". Claim 44 is objected to because DNA is misspelled as "DSN". Claim 55 is objected to because "Introduced" is capitalized.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41, 44, and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is indefinite in it recitation of "other proteins having [RGD] (arginine-glycine-aspartic acid) residues at one or both termini" and "other cell adhesion peptides". It is unclear what are the metes and bounds of these genuses. The phrase "other plasma proteins" precedes these phrases in the claims. Does Applicant intend to embrace only RGD and cell adhesion peptides that are not plasma proteins?

Claim 41 is also indefinite because it is unclear what are the metes and bounds of a "full or partial DNA constructs". The specification does not define the terms "full" or "partial" in this context, it is unclear what standard of comparison is to be applied when determining whether a DNA construct is complete or partial. Deletion of "full or partial" is suggested.

Claim 44 is indefinite because it is unclear what is intended by "and viral, liposomes, and cationic polymers." This claim is also indefinite because it appears that a period has been substituted for a comma immediately before "and viral", although this may be due to poor image quality in either the electronic copy of the claims, or in the copy supplied by Applicant.

Claim 46 is indefinite because although they are recited as alternatives, it is unclear what is the difference between a polypeptide and a protein.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 41 is drawn to the genus of plasma proteins (other than collagen, fibrinogen and vitronectin), growth factors, oligonucleotides, full or partial DNA constructs, natural or synthetic phospholipids, and polymers with phosphorylcholine functionality that have the effect of increasing cell attachment or thrombogenicity. The written description requirement may be satisfied for genus claims by disclosure of a representative number of species by reduction to practice or structural description, or by disclosure of relevant identifying characteristics such as a correlation between structure and function. The specification as filed does not disclose any examples any of the species set forth above. As a result, one of skill in the art could not conclude that Applicant was in possession of the clamed invention at the time of filing. It is noted that phosphorylcholine was recognized in the prior art as an antithrombogenic agent, and does not appear to promote cellular adhesion. See e.g. Bird et al (J. Biomed. 11:231-234, 1989) abstract.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 32, 33, 38, 39, 53-55, and 59 stand rejected under 35 U.S.C. 102(e) as being anticipated by Evans (US Patent 5,702,361).

Evans taught a system comprising embolizing polymer solutions in a biocompatible solvent and a non-particulate agent such as a metal coil. Preferred biocompatible polymers include cellulose diacetate and ethylene vinyl alcohol copolymer. In a preferred embodiment, the average molecular weight, as determined by gel permeation chromatography, of the cellulose diacetate composition is from about 25,000 to about 100,000 more preferably from about 50,000 to about 75,000 and still more preferably from about 58,000 to 64,000. See column 5, lines 40-48. Preferably, the polymer composition will comprise from about 2.5 to about 8.0 weight percent of the biocompatible polymer composition based on the total weight of the polymer composition. See column 7, lines 10-18. Both components of the system are considered to be biologically active inasmuch as they cause clot formation. See e.g. column 9, lines 27-33. The particular biocompatible polymer employed is not critical and is selected relative to the viscosity of the resulting polymer solution, the solubility of

the biocompatible polymer in the biocompatible solvent, the compatibility of the polymer composition with the non-particulate agent and the like. Such factors are well within the skill of the art. See column 5, lines 34-39. The biocompatible solvent can be an aqueous mixture comprising ethanol. See column 6, lines 44-52.

Evans also taught a method in which the non-particulate agent (e.g., platinum coils) is first introduced to the vascular site to be embolized via conventional catheter technology. After introduction of the non-particulate agent to the vascular site, a sufficient amount of the polymer composition is introduced by conventional means (e.g., catheter delivery under fluoroscopy). See column 8, lines 12-23.

Evans also taught kits comprising:

(a) a polymer composition comprising a biocompatible polymer, a biocompatible solvent and a contrast agent; and

(b) a non-particulate agent or plurality of such agents; or

(a) a prepolymer composition comprising a biocompatible prepolymer and a contrast agent; and

(b) a non-particulate agent or plurality of such agents.

Preferably, in either case, the kit further comprises a catheter capable of delivering said polymer or prepolymer composition.

Thus Evans anticipates the claims.

Response to Arguments

Applicant's arguments filed 8/4/06 have been fully considered but they are not persuasive.

Applicant asserts at page 6 of the response that the biologically active component recited in the claims is separate and distinct from the polymer-forming or dissolved polymeric material. In support of position Applicant indicates that listing the various components of the claim as items 'a', 'b', and 'c' clarifies that they are separate and distinct. This is unpersuasive because there is no reason that items 'a' and 'b' cannot be the same compound, or that items 'a' and 'b' cannot represent different fractions of a pool of a given compound.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32 and 34-36 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (US Patent 5,702,361) in view of Slepian (US Patent 5,634,946).

Evans taught a system comprising embolizing polymer solutions in a biocompatible solvent and a non-particulate agent such as a metal coil. Preferred biocompatible polymers include cellulose diacetate and ethylene vinyl alcohol

copolymer. In a preferred embodiment, the average molecular weight, as determined by gel permeation chromatography, of the cellulose diacetate composition is from about 25,000 to about 100,000 more preferably from about 50,000 to about 75,000 and still more preferably from about 58,000 to 64,000. See column 5, lines 40-48. Preferably, the polymer composition will comprise from about 2.5 to about 8.0 weight percent of the biocompatible polymer composition based on the total weight of the polymer composition. See column 7, lines 10-18. The particular biocompatible polymer employed is not critical and is selected relative to the viscosity of the resulting polymer solution, the solubility of the biocompatible polymer in the biocompatible solvent, the compatibility of the polymer composition with the non-particulate agent and the like. Such factors are well within the skill of the art. See column 5, lines 34-39.

Evans did not teach the use of polyesters or polyhydroxybutyrate as a biocompatible polymer.

Slepian taught a method for forming a biocompatible polymer coating on a tissue surface of a lumen in a body vessel, wherein the polymer is a biocompatible polymer selected from the group consisting of polymers and copolymers of hydroxycarboxylic acids, polyurethanes, polyesters, polyamides, polyacrylonitriles, polyphosphazenes, polylactones, polyanhydrides, polyethylenes, polyalkysulfones, polycarbonates, polyhydroxybutyrates, polyhydroxyvalerates, hydrocarbon polymers, polypropylenes polyvinylchlorides, ethylene vinyl acetates and combinations thereof. See claim 5. Slepian also taught that the polymers could be used to occlude a tissue lumen completely. See paragraph bridging columns 8 and 9.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use any of the polymers of Slepian in the method of Evans because these are considered to be recognized equivalents in the art of tissue lumen occlusion, and the invention of Evans is directed to occlusion of the lumens of blood vessels. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 8/4/06 have been fully considered but they are not persuasive.

Applicant asserts at page 6 of the response that the biologically active component recited in the claims is separate and distinct from the polymer-forming or dissolved polymeric material. In support of position Applicant indicates that listing the various components of the claim as items 'a', 'b', and 'c' clarifies that they are separate and distinct. This is unpersuasive because there is no reason that items 'a' and 'b'

cannot be the same compound, or that items 'a' and 'b' cannot represent different fractions of a pool of a given compound.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-41, 43, 44, 46 and 53-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okada et al (US Patent 5,202,352) in view of Cragg et al[1] (US 6,558,367 B1, May 6, 2003), Whalen et al (6,531,111 B1, March 11, 2003), Cragg et al[2] (6,146,373, 14 Nov 2000), Greff et al (6015541, 18 Jan 2000), Murayama et al (5,891,192, 6 April 1999), and Sawhney (US Patent 6,818,018).

Okada et al teaches a precursor composition that comprises different compositions, such as oils, salts of metals, wax, or synthetic or natural polymers, that include polypeptides, polysaccharides, poly-fatty acid esters, poly-amino acids, polyaldehydes, polyvinyl polymers, copolymer of lactic acid and glycolic acid etc. and a biologically active compound to from emboli in the vascular system (see claims 10-12) and the description in columns 7-9). The art also teaches molecular weight of the polymer to be in the range of 1,000 to 100,000 and concentration to be in 1 to 80% range (columns 7-11). The art also teaches that the composition could be administered

via catheter (see lines 1-25 in column 11) and different solvents. The art does not teach a composition comprising fibronectin.

At the time of the invention, references of record (Cragg et al[1], Cragg et al[2] , Whalen et al, Greff et al, Murayama et al, and Sawhney) taught embolizing compositions that comprised a precursor composition, a biocompatible solvent (such as dilute ethanol) and a therapeutic composition. These references also taught a wide variety of different polymers, which could be biodegradable or non-biodegradable polymers (see e.g. columns 5-6 in Greff et al, columns 5-6 in Whalen et al, columns 12-13 in Cragg et al[1], and columns 12 and 13 of Sawhney). The references also taught using catheter for delivery of the composition (e.g. Cragg et al[1]). It is noted that the embolizing compositions were used for delivery therapeutic compositions comprising a therapeutic protein or a radioisotope or other agents. Further, the art of record taught protein coating of occlusion coils for better adhesion to vascular cells and adhesion. For example, Murayama et al taught coating the occlusion coils with adhesion proteins, such as fibronectin (see column 2, lines 64-67, continued in lines 1-8 in column 3). The art of record also taught standardizing different parameters of the polymer, such as molecular weight, viscosity, concentration, particle size, etc.(see columns 5-8 in Whalen et al).

At the time of the invention, it would have been obvious to modify the composition of Okada et al and prepare compositions that have different polymers or different therapeutic proteins, such as fibronectin and have molecular weight of 10,000-100,000 and have 5 to 50% polymer concentration and comprised biocompatible

solvents, such as ethanol or DMSO and deliver the composition to a tissue with a catheter with a reasonable expectation of success. An artisan would have used fibronectin in the composition because such would have allowed adhesion of the embolizing composition to vascular tissue wall.

With regard to claims 56 and 57, Greff et al discuss the problem of premature polymerization in the catheter and to address this problem, they disclose the use of a barrier solvent to slow down the embolization process. See e.g. Accordingly, all the limitations are present in the cited references, and as noted in previous office actions, it would have been obvious to one of ordinary skill in the art to have utilized a kit comprising a polymer occlusion forming component, biologically active component and a biocompatible component or vaso-occlusive device or barrier plug to form an embolism in situ by delivering the composition via a catheter. One would have been motivated to provide a device and composition in vivo for the purpose of efficaciously applying a liquid solution wherein upon contact with blood a polymer forms occluding the vessel while also providing direct delivery of a therapeutic agent. As noted previously, there would have been a reasonable expectation of success because each of the claimed components had previously been demonstrated to be fabricated in such a manner that following an in vivo administration in a liquid form or viscous pre-polymer form with a therapeutic agent in a biocompatible solvent and contact with blood, a polymer formed sufficient to block blood flow (Greff et al and Okada et al).

Response to Arguments

Applicant's arguments filed 1/24/06 have been fully considered to the extent that they apply to the foregoing rejections, but they are not persuasive.

Applicant addresses the rejection over Evans and Slepian at pages 8 and 9 of the response, and the rejection over Evans and Murayama at page 10 of the response. Applicant argues that Evans fails to teach a biologically active agent. This is unpersuasive for the reasons set forth above, i.e. the polymer of Evans is considered to be biologically active clot formation is a biological process, and the polymer of Evans clot formation. See e.g. column 9, lines 27-33. Applicant also argues that there is no reasonable expectation of success, in either combination stating that one of skill in the art would not have expected success if he removed the non-particulate element of Evan's invention. This is unpersuasive because the rejections do not require that one remove the non-particulate element (i.e. the metal coil) from the invention of Evans. In fact, the rejection requires the opposite, that one retain the non-particulate element, because it corresponds to the mechanical occlusive device of the instant invention.

For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the

hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Peter Paras, can be reached at (571) 272-4517. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.
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